

REMARKS

Applicants' claimed invention is directed to a narrowly defined active compound combination consisting essentially of spiroxamine, prothioconazole (at a specific weight ratio range relative to spiroxamine) and tebuconazole (also at a specific weight ratio range relative to spiroxamine).

Rejection under 35 U.S.C. 103

Claims 9 and 11-15 stand rejected under 35 U.S.C. 103(a) based on U.S. Patent 5,789,430 ("Jautelat et al") in view of the cited Latteur et al article from *BioControl*, 47, 435-444 (2002) and further in view of U.S. Patents 6,503,932 ("Eicken et al") and 5,397,795 ("Valcke et al"). Applicants respectfully traverse.

As fully discussed in Applicants' previous Amendments, **Jautelat et al** discloses microbicidal triazolyl derivatives, one of which is prothioconazole. See, e.g., formula in Example 1 at column 35. Jautelat et al teaches that the disclosed compounds can be used in mixtures with other active compounds, including the fungicide tebuconazole (see column 33, line 21), but, despite providing exhaustive lists of possible mixing partners, does not mention spiroxamine. Moreover, Jautelat et al does not disclose mixtures of prothioconazole with any particular active ingredient mixing partner, much less suggest Applicants' very narrowly defined three-component composition. The Office Action relies on the other cited references to bridge these gaps between Jautelat et al and Applicants' invention. However, Applicants maintain that the other cited references would not lead those skilled in the art from Jautelat et al to their claimed invention. **Latteur et al** discloses efficacy data for twenty fungicides, among which are spiroxamine and tebuconazole (e.g., Table 2 at page 441), but specifically states at page 442 that "[a]ll fungicide formulations tested in this study contained a single active ingredient" (emphasis added) and that "[t]here are several questions about the possible effects of mixtures of two or three active ingredients at the same time," leaving open for further study using "improved tests" the answer to such questions. This is hardly the kind of teaching that would lead to efficacious combinations of active compounds, much less to the specific three-component combination claimed by Applicants. **Eicken et al** discloses fungicidal mixtures of certain biphenylamide compounds (an example of which is boscalid) and an amino compound described as being "spiroxamin" (but apparently represented by a defective formula). E.g., column 1, lines 4-40. Even if one assumes that the second compound is spiroxamine, the biphenylamide component shares

nothing in common with prothioconazole or tebuconazole, which are required by Applicants to complete their claimed three-component mixtures. **Valcke et al** discloses different binary fungicidal mixtures containing propiconazole (in contrast to prothioconazole) and tebuconazole. E.g., column 1, lines 28-32. Just as with Eicken et al, Valcke et al discloses mixtures containing only one of the compounds specified by Applicants. Furthermore, Applicants the Office Action provides no objective basis for using the absolute or relative amounts of the individual compounds used in the two-component mixtures taught by Eicken et al and Valcke et al to determine the relative amounts of spiroxamine, prothioconazole, and tebuconazole in a three-component mixture that would provide the enhanced efficacy found by Applicants. For these reasons alone, Applicants again submit that their claimed invention is not rendered obvious by Jautelat et al in view of the secondary references.

Applicants are, of course, aware the Supreme Court has set out a flexible approach to obviousness in *KSR International v. Teleflex*, 82 U.S.P.Q.2d 1385, 550 U.S. 398 (2007), but point out that the Supreme Court also recognized that a finding of obviousness still requires “articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” See 82 U.S.P.Q.2d at 1386 (quoting *In re Kahn*, 78 U.S.P.Q.2d 1329, 441 F.3d 977, 988 (Fed. Cir. 2006)). That is, something more than the mere disclosure of elements taken from the prior art is necessary to support an obviousness rejection. As explained by Judge Rader in a recent discussion of “obvious to try” analyses in *In re Kubin*, 90 U.S.P.Q.2d, 1417, 561 F.3d 1351 (Fed. Cir. 2009), the proper analytical framework requires the consideration of two classes of situations where “obvious to try” can be erroneously equated with obviousness, one of which applies when one varies disclosed parameters until possibly finding a successful result and the other of which applies when prior art gives only general guidance about a new technology or promising field of experimentation (in contrast to the predictable pursuit of known options to arrive at predictable solutions as contemplated by *KSR*). See *In re Kubin*, 90 U.S.P.Q.2d at 1423 (citing and quoting *In re O’Farrell*, 7 U.S.P.Q.2d 1673, 1681, 853 F.2d 894, 903 (Fed. Cir. 1988), as well as contrasting *KSR*). When considering the first situation, Judge Rader cautioned that “where a defendant merely throws metaphorical darts at a board filled with combinatorial prior art possibilities, courts should not succumb to hindsight claims of obviousness.” *In re Kubin*, 90 U.S.P.Q.2d at 1423 (emphasis added). Applicants submit that those skilled in the art – even though finding the

individual components of their claimed invention in the cited references by picking and choosing from among the host of possible compounds found in the cited references – would not have any expectation other than merely additive effects for any particular mixture. As expressed in several CAFC decisions handed down after *KSR*, unexpected properties continue to make for non-obviousness. For example, *Takeda Chemical Industries v. Alphapharm*, 83 U.S.P.Q.2d 1169, 492 F.3d 1350 (Fed. Cir. 2007), and *Sanofi-Synthelabo v. Apotex*, 550 F.3d 1075, 89 U.S.P.Q.2d 1370, 1379-1380 (Fed. Cir. 2008), both of which support the proposition that even under the liberal standards set forth in the *KSR* decision, obviousness can be overcome by evidence of unexpected properties.

Here, Applicants again refer to the objective evidence of nonobviousness found in their specification and in the previously submitted Declaration under 37 C.F.R. 1.132 of Dr. Peter Dahmen. By way of summary, Applicants again refer to Table 3 of their specification (which provides data showing that a three-component composition according to their invention exhibited 100% fungicidal efficacy against *Fusarium nivale*, whereas one would have expected a significantly lower efficacy of only 54% as calculated using the three-component Colby formula) and to the previously submitted Declaration (which shows that an inventive mixture of spiroxamine, prothioconazole, and tebuconazole was considerably more effective than at least some ternary mixtures containing compounds outside the scope of Applicants' claims). The direct evidence of synergism presented in the specification and the indirect evidence found in the Declaration led to an acknowledgement in the Advisory Action dated December 5, 2008, that Applicants had overcome the obviousness rejection of Claim 10, which differed from Claim 9 as then written only in specifying the limitations that Applicants subsequently incorporated into Claim 9 in the expectation of achieving allowance. However, since the current Office Action still criticizes their data as not being commensurate in scope with their claims, Applicants now submit a new Declaration of Dr. Dahmen to overcome this residual objection.

In particular, Dr. Dahmen's new Declaration presents data for compositions in which the relative amounts of the individual compounds vary over a much broader range than the 1:0.4:0.4 ratio of spiroxamine to prothioconazole to tebuconazole previously reported in Table 3 of the specification, namely at ratios of 1:1:1, 1:5:5, and 1:0.2:0.1. [Note that the order of quantities is presented differently in the Declaration.] In each experiment – including those of both the specification and the

new Declaration -- the inventive compositions always exhibited greater efficacy than would have been expected for purely additive effects. Applicants submit that this direct evidence of synergism is sufficient to overcome any inference of obviousness over the entire range claimed by Applicants.

Applicants therefore respectfully submit that their claimed invention is not rendered obvious by Jautelat et al in view of the cited Latteur et al article and further in view of Eicken et al and Valcke et al and, consistent with the representations in the previous Advisory Action, should be passed to allowance.

In view of the preceding amendments and remarks, allowance of the claims is respectfully requested.

Respectfully submitted,

By Richard E. L. Henderson
Richard E. L. Henderson
Attorney for Applicants
Reg. No. 31,619

Bayer CropScience LP
2 T.W. Alexander Drive
Research Triangle Park, NC 27709
Ph.: (919) 549-2183
Fax: (919) 549-3994

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